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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/597,946	09/01/2006	Roger Michael Lane	33659-US-PCT	8266

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CORPORATE INTELLECTUAL PROPERTY
ONE HEALTH PLAZA 104/3
EAST HANOVER, NJ 07936-1080

EXAMINER	
POLANSKY, GREGG	
ART UNIT	**PAPER NUMBER**
1614	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/597,946	LANE, ROGER MICHAEL	
	Examiner	Art Unit	
	GREGG POLANSKY	1614	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *10 October 2008*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1 and 3-19* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1 and 3-19* is/are rejected.

7)☒ Claim(s) *18* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Status of Claims

1. Applicant's response, filed 10/10/2008, to the Office Action mailed 4/10/2008 is acknowledged. Applicant canceled Claims 2 and 20-32, amended Claims 9-19, and presented arguments in response to the Office Action.

2. Claims 1 and 3-19 are pending and presently under consideration.

3. Applicant's arguments have been fully considered and are persuasive in part. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn. The following rejections and/or objections are either reiterated or newly applied. They constitute the complete set presently being applied to the instant application.

Claim Objections

4. Claim 18 is objected to because of the following informalities: Claim 18 recites "A method according to claim 17 wherein the cholinesterase inhibitor is rivastigmine tartrate (Exelon®) **and the anti-depressant is selected from rivastigmine tartrate (Exelon®), donepezil hydrochloride (Aricept®) and galanthamine hydrobromide (Reminyl®)** and the anti-depressant is selected from paroxetine hydrochloride…" (emphasis added). It appears that the claim has a typographical error, as highlighted above. Appropriate correction is required.

Claim Rejections - 35 USC § 103

5. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

6. Claims 1 and 3-19 are rejected under 35 U.S.C. 103(a) as being unpatentable over Roman et al. (The Lancet Neurology, 2002, Vol. 1, pages 426-436), in view of Seed, J. (U.S. Patent Application Pub. No. 2005/0143350 A1), and Hsu et al. (U.S. Patent Application Pub. No. 2002/0192243 A1).

Roman et al. teach clinical manifestations of vascular dementia include vascular depression. See page 431, 1st column, 2nd to last paragraph, and page 432, "Panel 3. Criteria for SIVD". Roman et al. disclose the use of cholinesterase inhibitors, including donepezil hydrochloride, rivastigmine tartrate, and galantamine hydrobromide, for the treatment of vascular dementia and the concomitant use of antidepressants, in particular serotonin-specific reuptake inhibitors (SSRIs) (e.g., sertraline and citalopram), for the treatment of depression which accompanies vascular dementia. See page 434, "Cholinesterase inhibitors" and "Other agents".

Although Roman et al. teach the combined use of a cholinesterase inhibitor (e.g., rivastigmine) and an antidepressant (e.g., setraline) for treating vascular depression, they do not teach a cholinesterase inhibitor and an antidepressant formulated together or the administration of rivastigmine by transdermal patch.

Seed teaches pharmaceutical compositions comprising at least one cholinesterase inhibitor, at least one antidepressant and a pharmaceutically acceptable carrier. See Abstract; page 5, paragraph 50; and page 22, claim 40. Seed teaches the instantly claimed cholinesterase inhibitors (i.e., donepezil, rivastigmine, galanthamine) and typical doses. See pages 2-3, paragraph 24 and page 3, paragraph 29. The reference teaches the dosages of the active agents are "in accordance with dosages and scheduling regimens practiced by those of skill in the art". Seed teaches, for example rivastigmine can be administered in a dose range of 0.4 mg to about 6.0 mg/dose and up to 12.0 mg/day. Seed teaches suitable antidepressant classes include *inter alia* tricyclics, SSRIs, SNRIs, and MAO inhibitors. Seed also teaches the instantly claimed individual antidepressants, such as sertraline, fluoxetine, venlafaxine, and citalopram. See for example, page 4, paragraphs 32 and 34. The reference teaches the composition may be administered by transdermal patch. See page 1, paragraph 12, and page 5, paragraph 51.

The reference by Hsu et al. is provided to demonstrate administration of cholinesterase inhibitors by transdermal patch was known at the time of the instant invention. The reference also teaches methods for enhancing the permeability of skin to transdermal application of cholinesterase inhibitors, while minimizing local skin irritation. See Abstract and page 6, paragraph 67. Hsu et al. teach transdermal patch surface area in the range of about 5-200 cm^2, which encompasses the range recited by instant Claims 14 and 15. See page 10, paragraph 101. The concentration of the drug (e.g., rivastigmine) is dependent on the desired daily dose to be administered, the size

of the patch and the flux rate of the drug. Hsu et al. also disclose that for transdermal administration, the cholinesterase inhibitor compounds should be "(1) an uncharged molecule, e.g., wherein a basic drug is in nonionized, free-base form, (2) a basic salt of an acidic drug, or (3) there are no additional species in the formulation or patch that could react with or be neutralized by the inorganic hydroxide, to any significant degree". See Abstract and page 5, paragraphs 43 and 44. Further, Hsu et al. disclose the instantly claimed cholinesterase inhibitor salts (i.e., donepezil HCl, galanthamine HBr, and rivastigmine tartrate). See page 6, paragraph 67.

As discussed *supra*, Seed or Hsu et al. do not teach a specific amount of rivastigmine in a transdermal patch of the sizes recited by instant Claims 7, 8, 14 and 15. However, Seed does teach the administration of rivastigmine in the same dose range as disclosed for the instant invention and Hsu et al. does teach a patch size range that encompasses the sizes recited for the instant invention.

It would have been well within the purview of one of ordinary skill in the art to formulate a transdermal patch to administer therapeutic doses of rivastigmine. One would have been so motivated to provide a more convenient method of administration, as well as a means of providing extended release of the medicament and improving patient compliance.

It would have been obvious to the skilled artisan to initiate administration of the active agents at a low dose and gradually increase the dose to a level that is determined by patient response and route of administration. One would have been

motivated to do so to effectively treat the patient while minimizing potential drug side effects.

The determination of both optimal dosage ranges and optimal modes of administration are parameters well within the purview of those skilled in the art through no more than routine experimentation. The determination of the optimum dosage regimen (i.e., patch composition amount and patch dimensions) to employ with the presently claimed active agents would have been a matter well within the purview of one of ordinary skill in the art.

Applicant argues that although Roman et al. teach vascular depression may be associated with vascular dementia, "vascular depression is not necessarily present in conjunction with vascular dementia" and that "Roman's disclosure of vascular dementia treatment is thus not a teaching of vascular depression treatment".

This argument is not persuasive. As discussed *supra*, Roman et al. teach treatment of vascular dementia and that vascular depression is a symptom of vascular dementia. Roman et al. teach the treatment of vascular dementia with cholinesterase inhibitors and antidepressants, including instantly claimed cholinesterase inhibitors such as donepezil, rivastigmine and galantamine, and instantly claimed antidepressants sertraline and citalopram. Since vascular depression is taught as occurring with vascular dementia (even if it doesn't occur all the time with vascular dementia), Roman et al. does teach treatment of vascular depression.

Finally, Applicant asserts "that one of ordinary skill in the art, when presented with the disclosures of Roman, Seed and Hsu at the time of the present invention,

would be motivated to use the combination of cholinesterase inhibitors and anti-depressants to treat vascular depression".

The Examiner disagrees. As discussed above, Roman et al. does teach the treatment of vascular depression. Seed and Hsu et al. provide teachings of dose ranges (which the artisan would use as a starting reference dose) and transdermal administration of the instantly claimed agents.

Conclusion

7. Claims 1 and 3-19 are rejected.

8. No claims are allowed.

9. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

10. Any inquiry concerning this communication or earlier communications from the examiner should be directed to GREGG POLANSKY whose telephone number is (571)272-9070. The examiner can normally be reached on Mon-Thur 9:30 A.M. - 7:00 P.M. EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ardin H. Marschel can be reached on (571) 272-0718. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Gregg Polansky/
Examiner, Art Unit 1614

/Ardin Marschel/
Supervisory Patent Examiner, Art Unit 1614